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To: Flowers, Lynn [Flowers.Lynn@epa.gov]
Subject: Carcinogenesis Table of Contents for November 1, 2016; Vol. 37, No. 11

Carcinogenesis Table of Contents Alert
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Biology, Genetics and Epigenetics

Editor's choice: Dual targeting of MDM2 with a novel small-molecule inhibitor overcomes TRAIL resistance in cancer
Anup Kumar Singh, Shikha S. Chauhan, Sudhir Kumar Singh, Ved Vrat Verma, Akhilesh Singh, Rakesh Kumar Arya, Shrankhla Maheshwari, Md. Sohail Akhtar, Jayanta Sarkar, Vivek M. Rangnekar, Prem M.S. Chauhan, and Dipak Datta
Carcinogenesis 2016 37: 1027-1040
http://carcin.oxfordjournals.org/content/37/11/1027.abstract?etoc
SummaryMost of the conventional MDM2 inhibitors interfere only at MDM2–p53 interaction and confer limited clinical application due to p53-mediated MDM2 transactivation. Here, we report a novel dual-targeting small-molecule inhibitor of MDM2 that overcomes TRAIL resistance in cancer.

TGF-β-induced stromal CYR61 promotes resistance to gemcitabine in pancreatic ductal adenocarcinoma through downregulation of the nucleoside transporters hENT1 and hCNT3
Rachel A. Hesler, Jennifer J. Huang, Mark D. Starr, Victoria M. Treboschi, Alyssa G. Bernanke, Andrew B. Nixon, Shannon J. McCall, Rebekah R. White, and Gerard C. Blobe
Carcinogenesis 2016 37: 1041-1051
http://carcin.oxfordjournals.org/content/37/11/1041.abstract?etoc
SummaryThe matricellular protein cysteine-rich angiogenic inducer 61 (CYR61) promotes resistance to the chemotherapy drug gemcitabine in pancreatic ductal adenocarcinoma cells by negatively regulating cellular uptake of gemcitabine through the nucleoside transporters hENT1 and hCNT3. Transforming growth factor-β (TGF-β)-Smad signaling induces CYR61 expression in stromal pancreatic stellate cells in the tumor microenvironment.

Honokiol suppresses pancreatic tumor growth, metastasis and desmoplasia by interfering with tumor–stromal cross-talk
Courey Averett, Arun Bhardwaj, Sumit Arora, Sanjeev K. Srivastava, Mohammad Aslam Khan, Aamir Ahmad, Seema Singh, James E. Carter, Moh'd Khushman, and Ajay P. Singh
Carcinogenesis 2016 37: 1052-1061
http://carcin.oxfordjournals.org/content/37/11/1052.abstract?etoc
SummaryThis study shows that Honokiol (HNK) decreases pancreatic tumor growth, metastases and associated desmoplasia. Mechanistically, HNK exerts these effects through downregulation of CXCR4 and SHH, which interferes tumor–stromal cross-talk. Together, these findings suggest that HNK can be used as a novel and effective agent for pancreatic cancer prevention and/or therapy.

Cancer Biomarkers and Molecular Epidemiology

Association of serum cotinine levels and lung cancer mortality in non-smokers
Raja M. Flores, Bian Liu, and Emanuela Taioli
Carcinogenesis 2016 37: 1062-1069
http://carcin.oxfordjournals.org/content/37/11/1062.abstract?etoc
SummaryBiomarkers of tobacco exposure show that unknown, involuntary sources of exposure to SHS are still present in USA, and may affect individual risk of death for cancer and other chronic diseases.

Effect of human papillomavirus seropositivity and E2F2 promoter variants on risk of squamous cell carcinomas of oropharynx and oral cavity
Yuncheng Li, Erich M. Sturgis, Ying Yuan, Meixia Lu, Xiaoli Cao, Qingyi Wei, and Guojun Li
Carcinogenesis 2016 37: 1070-1078
http://carcin.oxfordjournals.org/content/37/11/1070.abstract?etoc
SummaryThe modification of risk by either individual or combined risk genotypes of 5 polymorphisms were pronounced in never smokers than in smokers and in SCCOP but not in SCCOC. These findings indicate that the risk of HPV16-associated SCCOP was modified by E2F2 promoter variants, especially in never smokers.

Carcinogenesis

Downregulation of AIF by HIF-1 contributes to hypoxia-induced epithelial–mesenchymal transition of colon cancer
Zhong Xiong, Meng Guo, Yun Yu, Fei-Fei Zhang, Meng-Kai Ge, Guo-Qiang Chen, and Shao-Ming Shen
Carcinogenesis 2016 37: 1079-1088
http://carcin.oxfordjournals.org/content/37/11/1079.abstract?etoc
SummaryHypoxia negatively regulates AIF expression in colon cancer tissues and cell lines through HIF-1. As a result, downregulated AIF contributes to hypoxia-induced EMT by promoting oxidative inactivation of PTEN and activation of downstream Akt/GSK-3β/β-catenin signaling.

Silencing of ST6Gal I enhances colorectal cancer metastasis by down-regulating KAI1 via exosome-mediated exportation and thereby rescues integrin signaling
Yu Ri Jung, Jung-Jin Park, Yeung Bae Jin, Yuan Jie Cao, Myung-Jin Park, Eun Ju Kim, and Minyoung Lee
Carcinogenesis 2016 37: 1089-1097
http://carcin.oxfordjournals.org/content/37/11/1089.abstract?etoc
SummaryWe silenced the ST6Gal I gene in a metastatic SW620 CRC cell line and examined the metastatic behavior of the cells. Silencing of ST6Gal I increases CRC metastasis by reduction of KAI1 via exosome-mediated exportation, and thereby rescues integrin signaling.

Modeling mesothelioma utilizing human mesothelial cells reveals involvement of phospholipase-C beta 4 in YAP-active mesothelioma cell proliferation
Tatsuo Kakiuchi, Taishi Takahara, Yumiko Kasugai, Kotaro Arita, Noriaki Yoshida, Kennosuke Karube, Miyuki Suguro, Keitaro Matsuo, Hayao Nakanishi, Tohru Kiyono, Shigeo Nakamura, Hirotaka Osada, Yoshitaka Sekido, Masao Seto, and Shinobu Tsuzuki
Carcinogenesis 2016 37: 1098-1109
http://carcin.oxfordjournals.org/content/37/11/1098.abstract?etoc
SummaryThe disrupted Hippo pathway altered growth of immortalized human mesothelial cell lines in culture, conferring them with tumor-forming capability in mice. PLCB4 was involved in the growth of YAP-active, but not YAP-inactive, human mesothelioma cell lines in culture.

Significant interactions between maternal PAH exposure and single nucleotide polymorphisms in candidate genes on B[a]P–DNA adducts in a cohort of non-smoking Polish mothers and newborns
Shoba Iyer, Ya Wang, Wei Xiong, Deliang Tang, Wieslaw Jedrychowski, Stephen Chanock, Shuang Wang, Laura Stigter, Elzbieta Mróz, and Frederica Perera
Carcinogenesis 2016 37: 1110-1115
http://carcin.oxfordjournals.org/content/37/11/1110.abstract?etoc
SummaryWithin a Polish birth cohort, we explored interactions between maternal exposure to airborne polycyclic aromatic hydrocarbons (PAH) during pregnancy and maternal and newborn single nucleotide polymorphisms (SNPs) in plausible benzo[a]pyrene (B[a]P) metabolism genes on B[a]P-DNA adducts in paired cord and maternal blood samples. We observed significant interactions between maternal PAH exposure and SNPs on cord B[a]P-DNA adducts in the following genes: maternal CYP1A1 and GSTT2, and

newborn CYP1A1 and CYP1B1. These novel findings highlight differences in maternal and newborn genetic contributions to B[a]P-DNA adduct formation and have the potential to identify at-risk subpopulations who are susceptible to the carcinogenic potential of B[a]P.

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